



Are the Elderly More Susceptible to the Adverse Health Effects of PM?

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research
and
development

Background

- Epidemiological evidence indicates that some population groups are at higher risk from ambient air particulate matter (PM) compared to others.
- Groups considered at higher risk from PM exposure include the elderly and people with cardiovascular disease, diabetes, asthma and COPD.
- The underlying biological mechanisms and susceptibility factors which make these populations more at risk for adverse health effects following PM exposure are not well understood.

Science Questions

- Are the elderly at increased risk from particle air pollution?
- If so, what mechanism accounts for the increased risk after PM exposure?
- Can specific factors be identified that can identify specific populations or predict the likelihood of an individual is the health risk increased by interaction between PM and the aging process or by other diseases prevalent in the aged?

Are the elderly more susceptible to the adverse health effects of PM?

Age-Related PM _{2.5} -Associated Mortality				
City	Age group (yrs)	Total	Daily Deaths CVD	Daily Deaths Respiratory
London				
	15-64	29±6	10±3	2.4±2
	65-74	37±7	16±5	5±3
	>75	102±19	46±10	22±9
Rome				
	15-64	11±4	2.7±1.7	0.2±0.5
	65-74	13±4	4.5±2.3	0.6±0.8
	>75	30±8	16±5.1	2.2±1.7

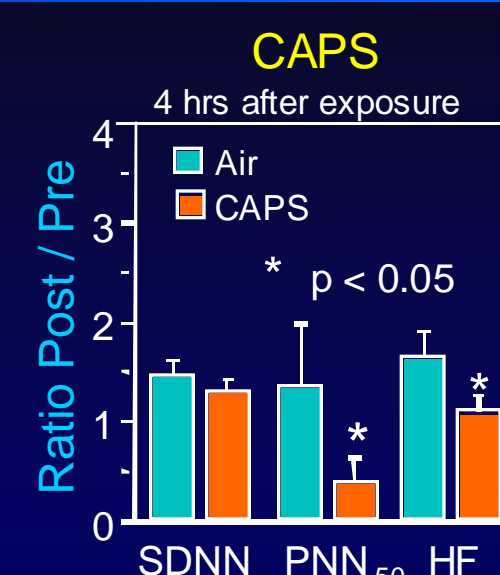
Aged-adults show increased susceptibility to the adverse health effects of PM exposure as determined by concentration-dependent increases in death and hospitalization.

PM_{2.5}-induced Changes in HRV in Aged Adults

Panel Studies
PM is associated with decreased HRV in the aged

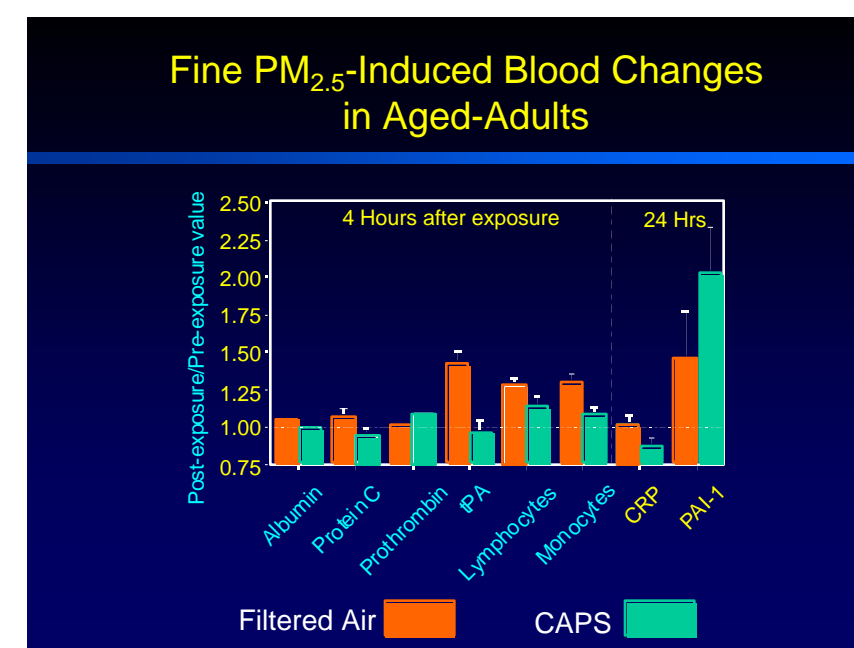
Baltimore
PM_{2.5} range 8 - 32 µg/m³
HF power B coefficient -0.012
95% confidence (-0.02 4, 0.000)

Boston
PM_{2.5} range 3 - 49 µg/m³
r-MSSD -6.1ms for 14.4 µg/m³
interquartile range

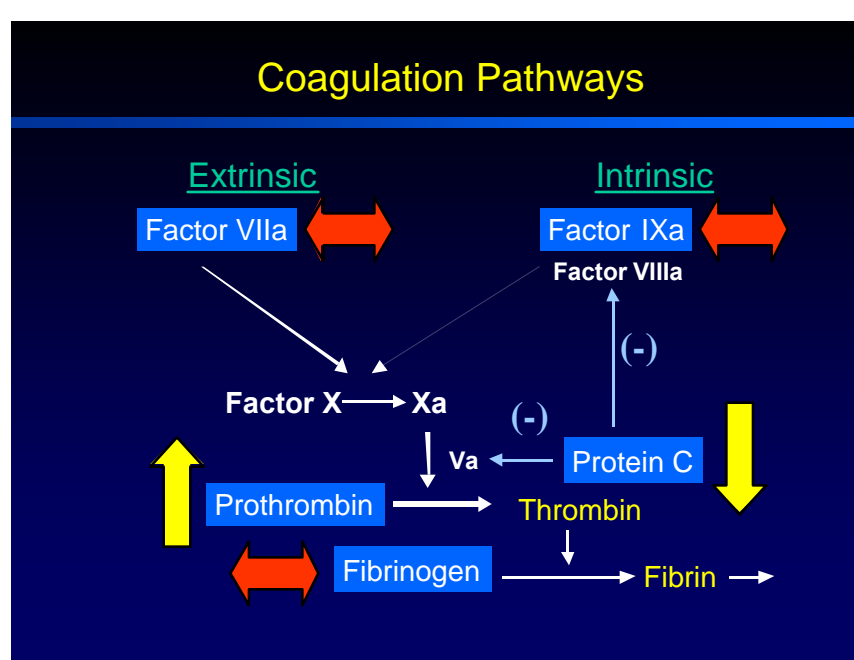


- Panel studies show an association between PM levels and decreased heart rate variability (HRV) with loss of vagal input (HF and r-MSSD). CAPS studies show a similar decrease in HF. They also show increased premature ventricular beats measured during the 24 hrs after exposure (data not shown).
- In contrast, no change in HRV or increases in arrhythmia were detected in healthy young-adults exposed to CAPS.

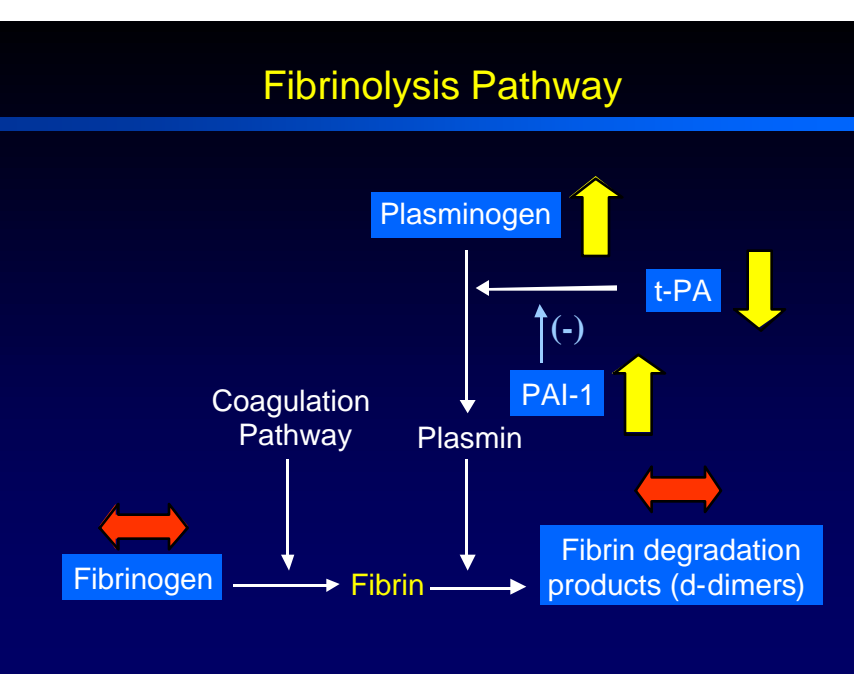
Does PM affect hemostatic proteins and inflammation in the elderly?



In aged-adults CAPS PM_{2.5} affected hemostatic proteins, circulating white blood cells and inflammatory markers.



CAPS PM_{2.5} decreased protein C and increased prothrombin.



CAPS PM_{2.5} increased plasminogen, and plasminogen activator inhibitor-1(PAI-1), and decreased tissue plasminogen activator (t-PA) in healthy elderly volunteers. Together, these changes suggest that exposure of the elderly to PM can lead to a more pro-thrombotic state.

Does PM worsen myocardial ischemia?

- PM increases ST segment depression during exercise an index of the degree of ischemia in humans having heart disease (Pekkanen J, et al. *Circ* 2002).
- This observation is relevant to aged-adults because over 65% of people ≥65 years old have cardiovascular disease.
- ST segment elevation is enhanced by CAPS exposure in dogs (Fig. 6.) implicating that exposure to PM worsens ischemia.

CAPS Increases ST Elevation in Ischemic Canine Hearts

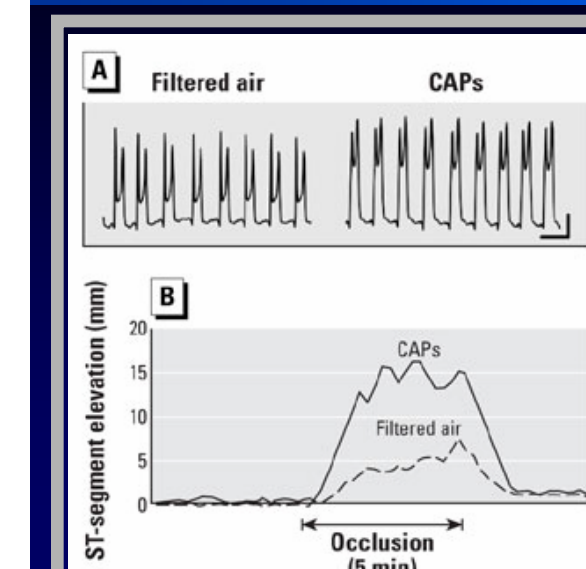
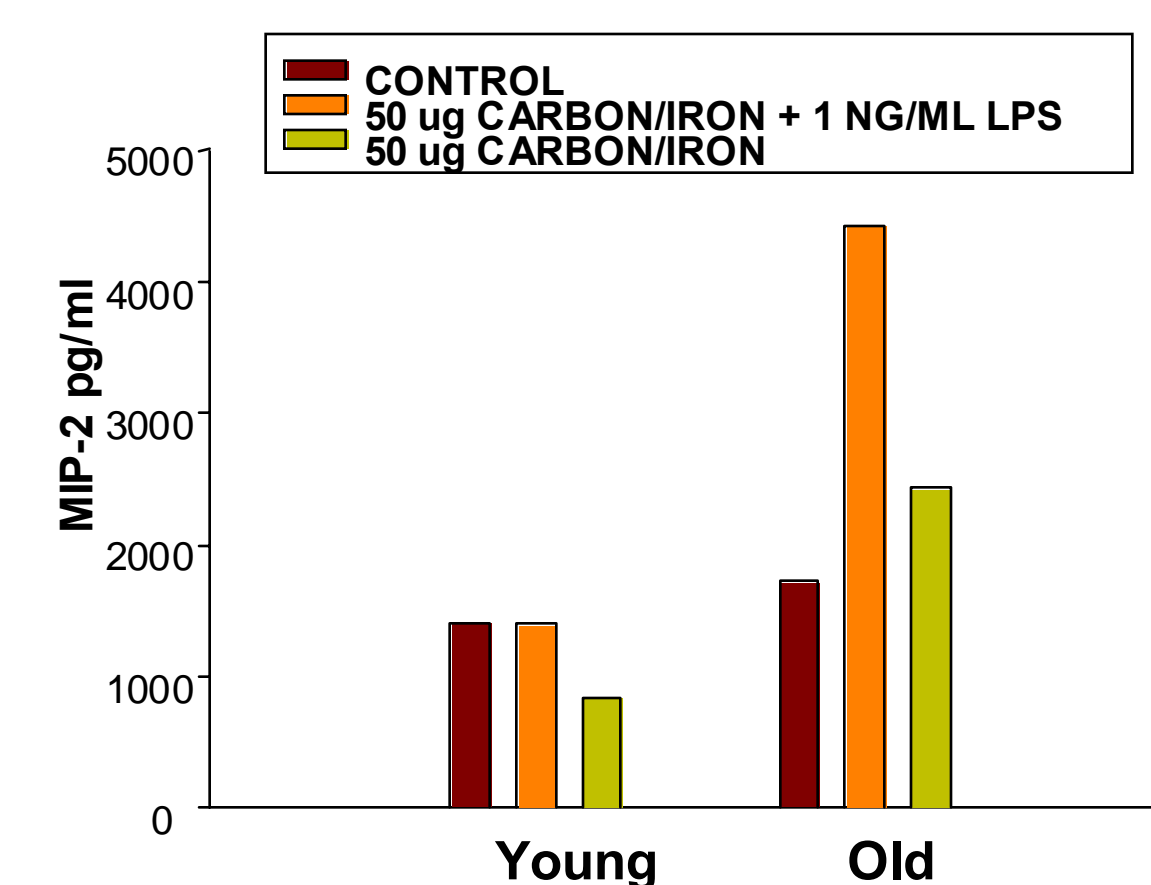


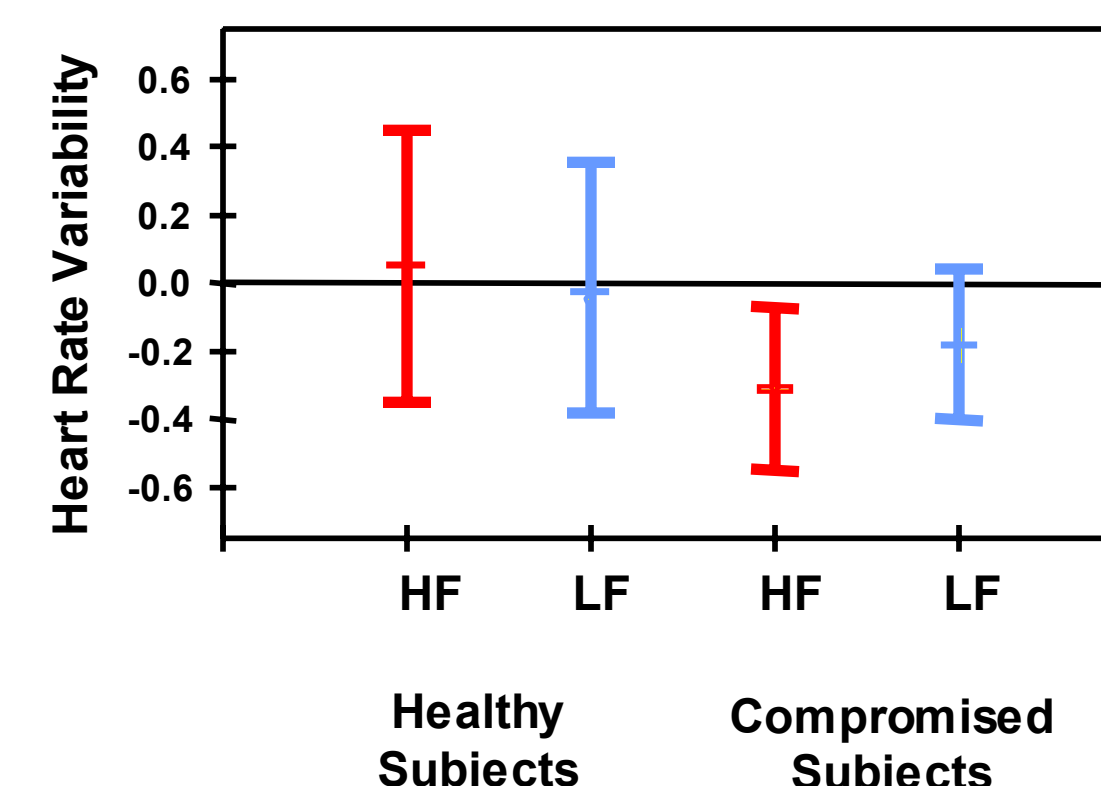
Fig. 6. (A) ECG tracings from a precordial lead exhibit an increase in ST-segment elevation in a dog during total occlusion of the LAD coronary artery after inhalation exposure to CAPS or filtered air (control). Horizontal bar = 50 ms; vertical bar = 5 mm. (B) Comparison of ST-segment elevation during 5-min LAD coronary artery occlusion in a dog after CAPS (solid line) and control (broken line) exposures.

Aged-adults lose the capacity to precondition, thus increased cardiac events in aged-adults associated with PM may reflect an imbalance between adverse and protective effects of PM.

Effect of Age on Macrophage MIP-2 Production in Aged Rats



Association Between PM and HRV in Elderly People with CV Disease



Results/Conclusions

- Particle air pollution, particularly in aged-adults, is associated with health risk possibly modulated through alterations of autonomic function, inflammation, oxidant stress and vascular dysfunction.
- PM exposure modifies several proteins involved in thrombosis. Some proteins favoring coagulation increase while fibrinolytic proteins decrease, suggesting a pro-thrombotic effect of PM exposure.
- Electrocardiographic evidence exists suggesting that PM exposure worsens myocardial ischemia. Some health effects are either more prominent or occur only in aged-adults confirming a greater sensitivity to the effects of PM in the aged.

Future Directions

- Characterize mechanisms accounting for the increased susceptibility of aged-adults to the effects of PM - particularly those having co-morbid conditions characterized by inflammation and increased oxidant stress (e.g. hypertension, diabetes, vascular disease and COPD).
- Determine whether the increased risk associated with PM exposure in the aged-adult population is caused by an increase in age-dependent process (e.g. decreased capacity to counter oxidant stress or precondition) or the increased prevalence of concomitant systemic diseases.
- Utilize novel genomic, proteomic and metabolomic methods to identify genetic susceptibility factors conferring increased protection or susceptibility to PM.

Impact and Outcomes

- Over 1 million American men and women die of heart disease, stroke, lung disease and diabetes each year. Each of these diseases is associated with a systemic inflammatory process and endothelial dysfunction.
- The data shown in this poster characterize some of the mechanisms by which PM can cause adverse health effects in the elderly, particularly those with pre-existing cardiopulmonary disease.
- Such knowledge will allow the development of a rational public health response, educational efforts, and regulatory policy to decrease PM-associated morbidity and mortality in the elderly.